

REMARKS

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date 4.10.03

By J. P. Isacson

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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 08-1641 for any such fees; and applicant(s) hereby petition for any needed extension of time.

MARKED UP VERSION ATTACHED TO AMENDMENT IN

SERIAL NO. 09/582,761

Marked up version of the paragraph starting at page 32, lines 1-8, is below:

Fuz12 (SEQ ID NO: 12) overlaps with Fuz11 at the 3' end by 14 bases and has the central region of fuzzy codons encoding C3d, but the 5' end of the oligonucleotide which represents the carboxy terminus of the gene contains a linker region (Gly-Gly-Gly-Gly-Ser **(SEQ ID NO: 47)** (in fuzzy codons), a *Bam*HI site, a stop codon and an *Eag*I site. The *Bam*HI site allows for subsequent fusion to the amino-terminal *Bgl*II site of another C3d domain for concatenation of multiple domain. The stop codon will be retained only in the carboxy-terminal C3d domains, and the *Eag*I site allows for subsequent cloning into the baculovirus vector pBacPak8.

Marked up version of the paragraph starting at page 39, lines 1-9, is below:

pBP66-08 was derived from pBP66-06 (see example 5), which is a baculovirus transfer vector containing a single copy of C3d-cys. A unique KpnI restriction site was engineered into the vector between the signal peptide and the C3d coding sequence to allow insertion of additional copies of the C3d sequence in which the additional copies of C3d differ from the original C3d sequence, and from each other by approximately 10% or more, but encode a polypeptide which is identical between residues Thr₁ and Pro₂₉₅, but may encode a linker or spacer sequence, such as the polypeptide sequence Ser-Ser-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Ser **(SEQ ID NO: 48)**, such as the fuzzy C3d monomer genes obtained using methods described in example 3.

Marked up version of the paragraph starting at page 39, lines 24-34, is below:

pBP67-08 contains an additional copy of C3d with variant sequence inserted at the KpnI site of pBP66-08. pBP66-08 contains two additional copies of C3d with variant sequence inserted at the KpnI site of pBP66-08. The sequence of the additional copies of C3d differ from the original C3d sequence, and from each other by approximately 10% or more, but encode a polypeptide which is

identical between residues Thr1 and Pro 295, but may encode a linker or spacer sequence, such as the polypeptide sequence Ser-Ser-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Ser-Gly-Ser (SEQ ID NO: 48). C3d monomers obtained using the methods described in example 3 are engineered to be inserted at the KpnI site by PCR amplification with the following primer pair: CGAGCCATATGGGTACCACCCCAGC (SEQ ID NO: 43) and GGTTAGCAGGTACCGGAACC (SEQ ID NO: 44) followed by digestion of the PCR product with the restriction enzyme KpnI.

Marked up version of the paragraph starting at page 42, lines 22-25, is below:

Example 8 A trifunctional linker reagent for coupling C3dcys and (C3d)n-cys to antigens

**N-Acetyl-Lys(N- ϵ -PDP)-Ala-Lys(N- ϵ -PDP)-Ala-Lys(N- ϵ -PDP)-OH (SEQ ID NO: 49)
(PDP=3-(2-pyridyldithio)propionyl, all-L)**